CLAIMS

WHAT IS CLAIMED IS:

1. A method for modulating the hypocretin system in an individual comprising administering a therapeutically effective amount of a preprohypocretin-expression modulator to the individual, wherein the preprohypocretin-expression modulator alters preprohypocretin expression in preprohypocretin-expressing cells.

2. The method of claim 1, wherein the modulator enhances preprohypocretin expression.

3. The method of claim 2, wherein the modulator binds to the 5' flanking promoter of the preprohypocretin gene.

4. The method of claim 1, wherein the modulator decreases preprohypocretin expression.

5. The method of claim 4, wherein the modulator binds to the 5'-flanking promoter of the preprohypocretin gene.

6. The method of claim 5, wherein the modulator is a cytokine.

7. The method of claim 6, wherein the cytokine is an interferon.

8. The method of claim 7, wherein the interferon is selected from the group consisting of alpha-interferon, beta-interferon, gamma-interferon, and combinations thereof.

9. The method of claim 8, wherein the interferon is alpha-interferon.

10. The method of claim 1, wherein modulation of the hypocretin system in the individual results in a change in the individual's sleep pattern.

11. The method of claim 10, wherein the individual suffers from a sleep disorder.

12. The method of claim 11, wherein the sleep disorder is an age-related sleep disorder.

13. The method of claim 11, wherein the sleep disorder is due to jet-lag.

14. The method of claim 10, wherein the modulator enhances preprohypocretin expression, thereby decreasing the individual's desire for sleep.

15. The method of claim 14, wherein the individual suffers from narcolepsy.

16. The method of claim 10, wherein the modulator decreases preprohypocretin expression, thereby increasing the individual's desire for sleep.

17. The method of claim 16, wherein the individual suffers from insomnia.

18. The method of claim 1, wherein the individual suffers from a mood disorder, chronic fatigue syndrome, or an attention deficit disorder.

19. The method of claim 1, wherein the individual suffers from neuronal degeneration resulting from prior ischemic events, and modulation of the hypocretin system alleviates said neuronal degeneration.

20. The method of claim 1, wherein the individual suffers from nausea or vomiting, and

modulation of the hypocretin system alleviates said nausea or vomiting.

21. The method of claim 1, wherein the individual suffers from irritable bowel syndrome, and modulation of the hypocretin system alleviates said irritable bowel syndrome.

22. The method of claim 1, wherein the individual suffers from incontinence, and modulation of the hypocretin system alleviates said incontinence.

23. The method of claim 1, wherein the individual suffers from visceral pain, and modulation of the hypocretin system alleviates said visceral pain.

24. The method of claim 1, wherein the individual suffers from an eating disorder, and modulation of the hypocretin system alleviates said eating disorders.

25. The method of claim 1, wherein the individual is a human.

26. The method of claim 1, wherein the preprohypocretin-expressing cell is located in the posterior lateral hypothalamus.

27. The method of claim 1, wherein the preprohypocretin-expressing cell is located in a peripheral tissue.

28. The method of claim 27, wherein the peripheral tissue is bladder tissue.

29. The method of claim 27, wherein the peripheral tissue is tissue comprising the gastrointestinal tract.

30. The method of claim 1, wherein the modulator is administered orally, parenterally, rectally, buccally, sublingually, nasally, by inhalation, topically, transdermally, intracerebralventricularly or via an implanted reservoir.

31. The method of claim 1, wherein the modulator is administered together with a pharmaceutically acceptable carrier as a pharmaceutical composition.

32. The method of claim 1, further comprising administration of one or more additional active agents.

33. The method of claim 32, wherein the additional active agent is selected from the group consisting of wakefulness-promoting drugs, tricyclic antidepressants, tetracyclic antidepressants, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and combinations thereof.

34. The method of claim 32, wherein the additional active agent is selected from the group consisting of modafinil, amphetamine, amphetamine homologues, caffeine, cocaine, cathinone, ephedrine, theophylline, theobromine, methylphenidate, dextroamphetamine, methamphetamine, pemoline, phenmetrazine, mazindol, selegiline, ritanserin, violoxazine, CRL40476, clomipramine, imipramine, desipramine, fluoxetine, paroxitine, sertraline, gammahydroxybutyrate, clonazepam, carbamazepine, yohimbine, and combinations thereof.

35. The method of claim 14, further comprising administration of one or more additional active agents.

36. A method of treating a narcoleptic patient comprising administering a therapeutically effective amount of a preprohypocretin-expression modulator to the individual, wherein the preprohypocretin-expression modulator enhances preprohypocretin expression in preprohypocretin-expressing cells located in the posterior lateral hypothalamus.

37. The method of claim 36, wherein the preprohypocretin-expression modulator binds to the 5' flanking promoter of the preprohypocretin gene.

38. The method of claim 37, wherein the preprohypocretin-expression modulator is a cytokine.

39. The method of claim 36, wherein the individual is a human.

40. The method of claim 36, further comprising administration of an additional active agent.

41. The method of claim 40, wherein the additional active agent is selected from the group consisting of amphetamine, amphetamine homologues, caffeine, cathinone, cocaine, ephedrine, methamphetamine, methylphenidate, modafinil, pemoline, phenmetrazine, and combinations thereof.

42. The method of claim 36, wherein the modulator is administered orally, parenterally, rectally, buccally, sublingually, nasally, by inhalation, topically, transdermally, intracerebralventricularly or via an implanted reservoir.

43. The method of claim 36, wherein the modulator is administered together with a pharmaceutically acceptable carrier as a pharmaceutical composition.

44. A method for identifying a compound that modulates the hypocretin system comprising contacting a test compound to cells equipped with the 5' flanking promoter of the preprohypocretin gene operably linked to a nucleic acid sequence and determining whether the test compound alters transcription of the nucleic acid sequence in the cells, wherein the test

compound's ability to alter transcription is indicative of a compound that modulates the hypocretin system.

45. The method of claim 44, wherein the cells are a naturally occurring preprohypocretin-expressing cells.

46. The method of claim 44, wherein the cells are genetically manipulated to be equipped with the 5' flanking promoter of the preprohypocretin gene.

47. The method of claim 46, wherein the nucleic acid sequence codes for a known gene.

48. The method of claim 47, wherein alteration of transcription is evidenced by a change in expression of the gene when compared to expression of the gene without the compound.

49. The method of claim 48, wherein the compound enhances expression of the gene.

50. The method of claim 49, wherein the compound binds to the 5'-flanking promoter of the preprohypocretin gene.

51. The method of claim 48, wherein the compound decreases expression of the gene.

52. The method of claim 51, wherein the compound binds to the 5'-flanking promoter of the preprohypocretin gene.

53. The method of claim 44, which is carried out *in vitro*.

54. An isolated DNA fragment coding for the 5' flanking promoter of the preprohypocretin gene.

55. The isolated DNA fragment of claim 54, comprising the nucleotide sequence of SEQ ID NO: 1.

56. An expression vector comprising the DNA fragment of claim 54.

57. The expression vector of claim 56, wherein the DNA fragment comprises the nucleotide sequence of SEQ ID NO: 1.

58. A host cell transformed with the expression vector of claim 56.

59. A compound that modulates the hypocretin system, wherein the compound is identified by the steps comprising contacting a preprohypocretin-expressing cell with the compound and determining whether the compound alters preprohypocretin expression in the preprohypocretin-expressing cell, wherein the compound's ability to alter preprohypocretin expression is indicative of a compound that modulates the hypocretin system.

60. A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 59.

61. The composition of claim 60, further comprising a pharmaceutically acceptable carrier.